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Evidence that renal vasodilation by dopamine in dogs does not involve release of prostaglandin

Renal vasodilation induced by the intra-arterial administration of dopamine has been attributed to activation of dopamine-specific receptors (Goldberg, 1972). Bell & Lang (1973) reported that electrical stimulation of areas in the midbrain of dogs produced renal vasodilation which was blocked by the dopamine receptor antagonist haloperidol, and suggested that the renal vasculature was innervated by nerves which released dopamine as a neurotransmitter.

Certain prostaglandins (PG), namely those of the A, B and E types, produce increases in renal blood flow (Higgins, Vatner & Braunwald, 1973; Lee, 1972; Marchand, Greenburg & others, 1973). Furthermore, PGE-like substances have been shown to be released from kidney in response to exogenously administered vasoactive substances such as angiotensin (McGiff, Crowshaw & others, 1970), bradykinin (Rogers, 1972) and noradrenaline (McGiff, Crowshaw & others, 1972). Release of PG in response to vasoconstrictor stimuli has been proposed as an intrinsic renal autoregulatory system (Sweet, Kadowitz & others, 1972; Aiken & Vane, 1973). If PG mediated the renal vasodilator effect of dopamine, then inhibition of PG synthesis might be expected to reduce or prevent increases in renal blood flow produced by dopamine. This hypothesis was examined by employing the non-steroidal anti-inflammatory drug indomethacin which has been demonstrated to block PG release (Davis & Norton, 1972; Aiken & Vane, 1973).

Mongrel dogs were anaesthetized with intravenously administered sodium pentobarbitone, 35 mg kg^{-1}. Left renal arterial blood flow was measured with an electromagnetic flowmeter (Biotronex); intra-arterial drug infusions were accomplished via an L-shaped 23-gauge needle inserted directly into the renal artery proximal to the site of application of the flow probe. Left renal blood flow and systemic arterial blood pressure (femoral artery) were recorded.

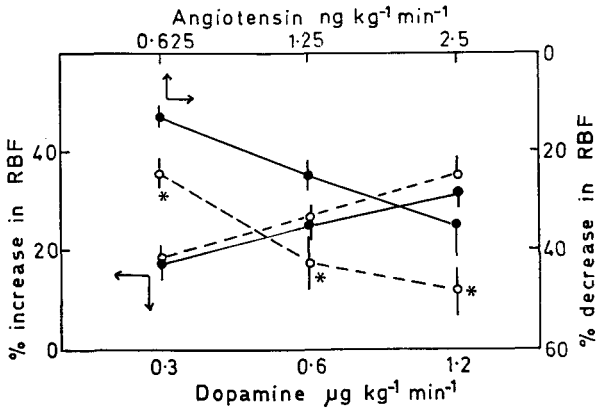

FIG. 1. Effects of indomethacin on changes in renal blood flow (RBF) induced by dopamine and angiotensin. Each point represents the mean of 5–6 values (± s.e.) $*P<0{\cdot}05$. —— Control responses. - - - After indomethacin.

Continous intrarenal arterial infusions of dopamine for 4–5 min at doses of 0·3, 0·6 and 1·2 $\mu g\ kg^{-1}\ min^{-1}$ produced dose-related increases in left renal blood flow, of 17·4 ± 2·7, 24·3 ± 2·8 and 31·2 ± 3·8% respectively, (mean ± s.e. of 5 or 6 dogs). Infusions of angiotensin reduced renal blood flow 13·6 ± 1·8, 25·2 ± 3·2 and 35·0 ± 7·0% at doses of 0·625, 1·25 and 2·5 ng $kg^{-1}\ min^{-1}$, respectively. When dopamine and angiotensin infusions were repeated 10–15 min after the intrarenal arterial injection of indomethacin, 2 mg kg^{-1}, statistically significant increases in the vasoconstrictor responses to all 3 doses of angiotensin occurred, but vasodilator responses to dopamine were essentially unaltered (Fig. 1). Our results thus provide indirect evidence that renal vasodilatation in response to dopamine is not apparently dependent upon release of prostaglandins. We also confirmed the observations of Aiken & Vane (1973) that indomethacin potentiates the vasoconstrictor effect of angiotensin in the canine kidney.

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